(9)

PATENT

Docket No. 1377-0137P

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS:	John Kevin Collins *et al.*	
APPLN. NO.:	09/367,105	GROUP: 1651
FILED:	November 10, 1999	EXAMINER: I. Marx
FOR:	PROBIOTIC STRAINS FROM LACTOBACILLUS SALIVARIUS AND ANTIMICROBIAL AGENTS OBTAINED THEREFROM	

DECLARATION UNDER 37 C.F.R. § 1.32

Assistant Commissioner of Patents

Washington, DC 20231

Sir:

I, Peter A. Anton, M.D., a U.S. citizen, am presently employed at UCLA School of Medicine, at MRL 2734, 675 Charles E. Young Dr. South, Los Angeles, CA 90095, USA, where I am Associate Professor of Medicine and the Director of the Center for HIV and Digestive Diseases. My *Curriculum Vitae* is attached hereto. I do solemnly and sincerely declare as follows:

1. I have read the Office Action dated June 19, 2001, each of the three cited references and a copy of the specification of the above U.S. Application.

2. I have also read a draft of the Declaration to be made by Dr. Liam O'Mahony by way of response and I fully agree with the statements contained in that Declaration as regards the cited references relied on by the Examiner.

3. In my view that novel and inventive approach taken by Collins *et al.* to isolate *Lactobacillus salivarius* strains with potential application to human healthcare was unprecedented.

4. The stains of *Lactobacillus salivarius* isolated by Collins *et al.* from appendices and sections of the large and small intestine of the human gastrointestinal tract obtained during reconstructive surgery represents a significant departure from previous methods for isolating probiotic bacteria.

I hereby declare that all statements made herein of my own knowledge are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the Application or any patent issued thereon.

December 6, 2001 _____

Date Peter A. Anton

CURRICULUM VITAE
PETER A. ANTON, M.D.

BUSINESS ADDRESS: University of California at Los Angeles (UCLA)
Department of Medicine
Division of Digestive Diseases
Mucosal Immunology
MRL 2734, Los Angeles, CA 90095
Telephone: (310) 206-5797
Appointments: (310) 825-1597
FAX: (310) 206-8824
email: panton@mednet.ucla.edu

HOME ADDRESS: 7777 Hollywood Boulevard,. #309
Los Angeles, CA 90046
Telephone: (323) 855-0188
FAX: (323) 512-7237

DATE OF BIRTH: November 14, 1954

PLACE OF BIRTH: Indianapolis, Indiana

CITIZENSHIP: USA

SOCIAL SECURITY: 569-04-4498

EDUCATION:

1986-1989	Gastroenterology Fellowship UCLA Combined GI Training Program, UCLA Los Angeles, California
1984-1986	Internal Medicine Residency Brigham and Women's Hospital, Harvard Medical School Boston, Massachusetts
1983-1984	Internal Medicine Internship Brigham and Women's Hospital, Harvard Medical School Boston, Massachusetts
1978-1983	MD Case Western Reserve University School of Medicine Cleveland, Ohio
1980-1981	Pathology Fellowship Institute of Pathology University Hospitals, CWRU School of Medicine Cleveland, Ohio

1978	Rotary Foundation Fellowship Environmental Sciences University of New Zealand Auckland, New Zealand
1973-1977	BA (magna cum laude) Harvard College Cambridge, Massachusetts Major: *Biology*; Minor: *Vertebrate Paleontology*

LICENSURE: California (G-56998)

BOARD CERTIFICATION:

Internal medicine - board eligible
Gastroenterology - eligible with IM boards

PROFESSIONAL EXPERIENCE:

1997- present	Associate Professor of Medicine, UCLA
1989 - 1996	Assistant Professor of Medicine, UCLA
1986-1989	Fellow in Gastroenterology, UCLA

PROFESSIONAL ACTIVITIES:

Administrative:

1995 - present	Director UCLA Center for HIV and Digestive Diseases
1994-1997	Director IBD Case Conference (weekly fellow's conference)
1992 – 1997	Director UCLA Inflammatory Bowel Disease Clinical and Research Center
1991 - 1997	Director: Clinical Trials UCLA IBD Clinical and Research Center
1990 – 1992	Associate Director UCLA Inflammatory Bowel Disease Clinical and Research Center

Committee service:

January 20001 - present	Centers for Disease Control, Atlanta, GA Invited Member, Rectal Microbicide Clinical Trials Design
2000 – present	UCLA Mind Body Collaborative Research Center Consultant, Neuro-Immune Interactions
2000 – present	UCLA Health Psychology Training Grant Faculty Instructor

October 2000	NIH Office of AIDS Research Invited Member, Committee for Comprehensive Plan for Microbicidal Research (Workshop)
1999 - present	ACTG Mucosal Immunology Focus Group (Immunology RAC) Member
1998 – present	UCLA Medical School Division of Digestive Diseases Division Budgetary Committee
July 1998	XII International Conference on AIDS, Geneva International Abstract Reviewer
1997 – present	CURE/UCLA Clinical Symposium Executive Planning Committee
1997 – present	UCLA Medical School Division of Digestive Diseases Director: HIV Mucosal Immunology Section
1996 – present	AIDS ReSearch Alliance, West Hollywood, CA Community Clinical Trials Medical Executive Committee
1996 – present	UCLA Medical School Division of Digestive Diseases Clinical Trials Group
1996 – 1998	RAND - UCLA HCSUS (Health Costs Services Utilization Study for HIV) Managed Care Focus Group for Physicians treating patients with HIV
1996 – 1997	UCLA Medical School Advanced Clinical Diagnosis for Medical Students Instructor
July 1996	XI International Conference on AIDS, Vancouver International abstract reviewer
19995 – present	UCLA Coordinated GI Training Program Lecturer/Coordinator on mucosal immunology, IBD, HIV
19995 – present	University-wide AIDS Research Council (UC): Clinical Sciences Program
1994 – present	UCLA Medical School Division of Digestive Diseases Faculty Recruitment/Selection Committee
1994 – 1997	UCLA Internal Medicine Board Review Course Infectious and Inflammatory Diarrhea Syllabus and Lecture
1994 – 1997	UCLA Medical School Division of Digestive Diseases Finance Committee Member
1994 – 1996	UCLA Medical School Division of Digestive Diseases Section Head: Mucosal Immunology
1993 – present	CURE: Center for Gastroenteric Biology Grant Reviewer

1993 – present	UCLA Dean's Task Force on Psychoneuroimmunology Executive Committee
1993 – 1997	Division of Gastroenterology CURE Executive Advisory Committee
1990 – present	Norman Cousins Program in Psychoneuroimmunology Member
1990 – 1994	GI NIH Training Grant, Executive Committee Member
1989 – 1992	Division of Gastroenterology: Education Committee
1989 – 1990	Executive Committee UCLA/Harbor IBD Center

Community Service:

1989 - 1999	Venice Family Clinic Venice, California Volunteer Physician
1989 - 1994	Raymond Alf Museum of Natural History Board of Trustees Member
1980 - 1981	Jubilee Refugee Camp Kowloon, Hong Kong Volunteer Medical Assistant
1978 - 1983	Cleveland Free Clinic Cleveland, Ohio Volunteer Medical Student

Professional Societies:

1997- present	American Gastroenterology Association
1995- present	Crohn's and Colitis Foundation
1992- present	Society for Mucosal Immunology
1991- present	International Society for Neuroimmunomodulation
1990- present	Clinical Immunology Society
1989- present	American Association for the Advancement of Science
1989- present	American College of Physicians - associate member
1989- present	American Federation for Clinical Research
1986- 1999	Alpha Omega Alpha

Journal Reviewer:

AIDS
American Journal of Medicine
American Journal of Pathology
Cytometry
Digestive and Liver Disease
Immunology Letters
Journal of AIDS
Journal of Leukocyte Biology
Journal of Virology
The AIDS Reader
The Histochemical Journal

HONORS AND SPECIAL AWARDS:

1983	Alpha Omega Alpha
1978	Rotary Fellowship, University of Auckland, New Zealand
1977	Magna cum laude, Harvard University
1974-1976	University Scholar, Harvard University

RESEARCH GRANTS:

AGENCY	PROJECT TITLE	ROLE	PERIOD from-to	TOTAL AWARDED
BASIC RESEARCH GRANTS				
NIH	Immunology training grant	Fellow	7/86-6/87	$40,000
Blinder Foundation	Role of substance P in Crohn's disease	Fellow	7/86-6/88	$80,000
UCLA/Norman Cousins: PNI pilot grant	Neuroendocrine regulation of the mucosal immune system	Co-PI	7/87-6/89	$30,000
CCFA (Crohn's & Colitis Foundation of America)	Role of substance P receptor in gut inflammation (Research Career Development Award)	PI	7/88-6/89	$85,000
NIH	Neuroimmunomodulation in human gut mucosa (Physician Scientist Award-DK01879)	PI	7/89-6/94	$364,000
NIH/CURE	Chemical characterization of H. Pylori chemotactic factor (Pilot and feasibility grant)	PI	7/92-6/93	$18,000
NIH/CURE	Chemical characterization of H. Pylori chemotactic factor (Pilot and feasibility grant-RENEWAL)	PI	7/93-6/94	$13,000

AGENCY	PROJECT TITLE	ROLE	PERIOD from-to	TOTAL AWARDED
NIH	Mucosal lymphocyte phenotype in early HIV infection (supplemental award to AIDS Institute Grant- I. Chen (PI), directed to Anton)	PI	7/94-6/95	$107,000
Doornbos Foundation	Role of stress in inflammatory bowel disease	PI	2/94-2/96	$100,000
Bing Foundation	Psychoneuroimmunology and the inflammatory response	PI	7/94-6/97	$1,101,000
NIH	Role of the gp120 VH3 superantigen in HIV-1 pathogenesis (J. Braun - PI)	Co-PI	9/95-8/96	($625,456) $14,600
Norman Cousins Program in PNI	Hypothalamic modulation of GI inflammation (Pilot & Feasibility)	PI	7/95-6/96	$14,500
Norman Cousins Program in PNI	Hypothalamic modulation of GI inflammation (renewal)	Co-PI	7/96-6/97	$18,500
AIDS Institute UCLA (CFAR:Center for AIDS Research)	Quantification of intestinal mucosal HIV-1 viral load (Pilot & Feasibility)	PI	7/96-6/97	$28,500
AIDS Institute CFAR	Mucosal Immunology CORE Director	PI (Core)	7/98-6/03	$250,000
UARP: ACRC (PI: Mitsuyasu)	Is HIV infection a mucosal inflammatory disease?	PI (project)	7/99-6/02	$298,000
amfAR	Novel mucosal route for HIV vaccine	PI	7/99-6/01	$150,000
NIH	K24 Award: Impact of co-receptor and HIV viral burden on gut mucosa	PI	4/00-3/05	$540,000
CLINICAL RESEARCH GRANTS				
MMD (Marion Merrell Dow)	Treatment of inflammatory bowel disease with oral Pentasa: Compassionate requests for Crohn's disease	PI	6/92-9/93	$4,000
ASTRA-DRACO (Besselaar)	42-day, double blind, parallel group, multicenter study comparing safety and efficacy of three dose levels Budesonide (enema) with placebo in ulcerative colitis	PI	7/92-6/93	$22,100

AGENCY	PROJECT TITLE	ROLE	PERIOD from-to	TOTAL AWARDED
Abbott Labs	Safety and efficacy of Zileuton vs. placebo for 8 weeks in ulcerative colitis	PI	7/92-6/93	$18,105
ASTRA-DRACO (Besselaar)	Open label optional extension period for Budesonide enema in ulcerative colitis	PI	7/92-5/94	$14,000
Salix	Randomized, placebo controlled, double blind comparison of two doses of Colazide (balsalazide) in ulcerative colitis	PI	8/93-3/95	$43,897
Abbott Labs	Long term safety and efficacy of Zileuton in ulcerative colitis	PI	9/93-6/94	$19,774
NIH/CFAR	Role of early, aggressive endoscopy in the evaluation of HIV-related diarrhea (pilot and feasibility grant)	PI	1/94-1/95	$9,500
MMD (Marion Merrell Dow)	Efficacy and safety of oral Pentasa in active Crohn's disease	PI	1/94-4/95	$45,200
Salix	Open label evaluation of Colazide (balsalazide) for maintenance therapy in ulcerative colitis	PI	3/94-6/95	$35,834
ASTRA	An international study to assess health related quality of life and its predictors in inflammatory bowel disease (IBDQ)	PI	1/96-11/96	$7,400
ASTRA	Budesonide controlled ileal release capsules in Crohn's disease- a placebo controlled maintenance trial	PI	1/96-6/97	$15,850
ASTRA	Budesonide controlled ileal release capsules in active Crohn's disease- a placebo controlled trial	PI	1/96-6/97	$62,000
Ross/ABBOTT	A placebo controlled study of an oral nutritional supplement in patients with ulcerative colitis	PI	1/96-9/97	$64,497
MACY'S West Foundation	Development of a clinical research center focused on the gastrointestinal effects of HIV	PI	1/97 – 1/00	$450,000

AGENCY	PROJECT TITLE	ROLE	PERIOD from-to	TOTAL AWARDED
Cell Genesys	A phase II study of the activity and safety of autologous CD4-zeta gene-modified T cells with or without exogenous IL-2 in HIV infected patients -A9602 ADDENDUM study to evaluate tissue response	PI (tissue study)	8/97	$18,200
Norman Cousins Program in PNI	Maximizing healing: Ayurvedic meditation and yoga for adolescents and young adults with ulcerative colitis	Invest.	12/97	$100,000
Pfizer	Leukotriene receptor antagonist (CP-195,543): a placebo controlled trial in ulcerative colitis	PI	1/98	$26,490
Cell Genesys	A phase II study of autologous CD4-zeta gene-modified T cells in HIV-infected patients with undetectable plasma viremia on HAART, A9801 ADDENDUM study to evaluate tissue response	PI (tissue study)	3/98	$32,300
Cell Genesys	A phase II study of autologous CD4-zeta gene-modified T cells in HIV-infected patients with undetectable plasma viremia on HAART, A9801: National Center for Tissue Processing HIV RNA and DNA	PI	3/98	$226,352
Celgene	Compassionate use of thalidomide in adults with HIV-associated wasting.	PI	4/98	0
AIDS ReSearch Alliance	Quantitation of tissue viral load (RNA and DNA) in subjects with undetectable plasma viremia at 3 month intervals for 1 year	PI	4/98	$25,000
Procter & Gamble Pharmaceuticals	A randomized, double blind, placebo-controlled, parallel design pilot study of Asacol 4.8 gr/day administered orally in HIV-positive males on stable anti-viral therapy	PI	6/99 – 1/01	$1,245,661
Campbell Foundation	Novel use of thalidomide to decrease total body HIV-1 viral burden	PI	5/00 – 4/01	$88,403

AGENCY	PROJECT TITLE	ROLE	PERIOD from-to	TOTAL AWARDED
UCLA AIDS Institute (CFAR)	Comparative efficacy of different immunization sites in eliciting mucosal immune responses to HIV-1	PI	1/01 – 6/30/01	$100,000
NIH/NIAID	Role of immunization site in eliciting mucosal immunity.	PI	7/1/01-6/30/04	$750,000

PUBLICATIONS:

A. RESEARCH PAPERS - Peer Reviewed

1. Ng WS, PA Anton and K Arnold. *Neisseria gonorrhea* strains isolated in Hong Kong: *In vitro* susceptibility to 13 antibiotics. **Antimicrob. Agents Chemother.** 19:12-17, 1981.
2. Jacobs MR, JF Tomashefski, A Franco, and PA Anton. Penicillin susceptibility testing of gonococci by disc diffusion. **J. Antimicrob. Chemother.** 7:319-330, 1981.
3. Anton PA, JA Kemp, T Butler and MR Jacobs. Comprehensive efficacies of ceftriaxone, moxalactam and ampicillin in experimental *Salmonella typhimurium* infection. **Antimicrob. Agents Chemother.** 22:312-315, 1982.
4. Anton PA and C Abramowsky. Adult polycystic renal disease presenting in infancy: A report emphasizing the bilateral involvement. **J. Urol.** 128:1290-1291, 1982.
5. Butler T, B Dahms, K Lindpainter, M Islam, MAK Azad, PA Anton. Segmental necrotizing enterocolitis: pathological and clinical features of 22 cases in Bangladesh. **Gut** 28:1433-1438, 1987.
6. Anton PA, SR Targan, SR Vigna, M Durham, AD Schwabe, F Shanahan. Enhanced neutrophil chemiluminescence in Familial Mediterranean Fever. **J. Clin. Immunol.** 8:148-156, 1988.
7. Shanahan F, PA Anton. Neuroendocrine modulation of the immune system. Possible implications for inflammatory bowel disease. **Dig. Dis. Sci.** 33:41S-49S, 1988.
8. Anton PA, SR Targan, F Shanahan. Increased neutrophil receptors for and response to the proinflammatory bacterial peptide FMLP in Crohn's disease. **Gastroenterology** 97:20-28, 1989.
9. Shanahan F, A Niederlehner, N Carramanzana, PA Anton. Sulfasalazine inhibits the binding of TNF_a to its receptor. **Immunopharmacology** 20:217-224, 1990.
10. Anton PA, JR Reeve Jr., JE Rivier, A Vidrich, W Schepp, F Shanahan. Biotinylation of a bombesin/gastrin-releasing peptide analogue for use as a receptor probe. **Peptides** 12:375-381, 1991.
11. Anton PA, JR Reeve, A Vidrich, E Mayer, F Shanahan. Development of a biotinylated analogue of substance P for use as a receptor probe. **Lab. Invest.** 64:703-708, 1991.
12. Martin FC, PA Anton, JA Gornbein, F Shanahan, JE Merrill. Production of interleukin-1 by microglia in response to substance P: role for a non-classical NK-1 receptor. **J. Neuroimmunol.** 42:53-60, 1993.

13. Shanahan F, PA Anton. A potential role for the immune system in gastric acid secretion and peptic ulcer disease. **Gastroenterology** 104:1874-1881, 1993.
14. Anton PA, F Shanahan, XP Sun, D Diehl, A Kodner, EA Mayer. VIP modulates intracellular calcium oscillations in human lymphoblasts. **Immunopharmacol. Immunotoxicol.** 15:429-446, 1993.
15. Bernstein CN, L Artinian, PA Anton, F Shanahan. Low-dose 6-mercaptopurine in inflammatory bowel disease is associated with minimal hematologic toxicity. **Dig. Dis. Sci.** 39:1638-1641, 1994.
16. Mitrovic B, FC Martin, AC Charles, LJ Ignarro, PA Anton, F Shanahan, JE Merrill. Neurotransmitters and cytokines in CNS pathology. **Prog. Brain Res.** 103:319-330, 1994.
17. Bernstein CN, LL Seeger , JW Sayre, PA Anton, L Artinian, F. Shanahan. Decreased bone density in inflammatory bowel disease is related to corticosteroid use and not disease diagnosis. **J. Bone Miner. Res.** 10:250-256, 1995.
18. Bernstein CN, F Shanahan, PA Anton, W Weinstein. Patchiness of mucosal inflammation in treated ulcerative colitis: a prospective study. **Gastrointest. Endosc.** 42:232-237, 1995.
19. Bernstein CN, LL Seeger, PA Anton, L Artinian, S Geffrey, W Goodman, TR Belin, F Shanahan. A randomized, placebo-controlled trial of calcium supplementation for decreased bone density in corticosteroid-using patients with inflammatory bowel disease: a pilot study. **Aliment. Pharmacol. Ther.** 10:777-786, 1996.
20. Porter EM, L Liu, A Oren, PA Anton, T Ganz. Localization of human intestinal defensin 5 in Paneth cell granules. **Infect. Immun.** 65:2389-2395, 1997.
21. McGowan I, PA Anton. AIDS and intestinal disease. **Curr. Opinion Gastroenterol.** 13:18-23, 1997.
22. Ilnyckyj A, F Shanahan, PA Anton, M Cheang, CN Bernstein. Quantification of the placebo response in ulcerative colitis. **Gastroenterology** 112:1854-1858, 1997.
23. McGowan I, RM Fairhurst, F Shanahan, PA Anton. Mucosal substance P receptor expression in HIV infection and inflammatory bowel disease. **Neuroimmunomodulation**, 4:70-76, 1997.
24. Anton PA, J O'Connell, D O'Connell, L Whitaker, GC O'Sullivan, JK Collins, F Shanahan. Mucosal sub-epithelial binding sites for the bacterial chemotactic peptide, formyl-methionyl-leucyl-phenylalanine (fMLP). **Gut** 42:374-379, 1998.
25. Anton PA, F Shanahan. Neuroimmunomodulation in inflammatory bowel disease: how far from "bench" to "bedside"? **Ann. N. Y. Acad. Sci.** 840:723-734, 1998.
26. Goode T, J O'Connell, C Sternini, PA Anton, H Wong, GC O'Sullivan, JK Collins, F Shanahan. Substance P (NK-1) receptor is a marker of human mucosal but not peripheral mononuclear cells: molecular quantitation and localization. **J. Immunol.** 161:2232-2240,1998.
27. M Million, Y Taché, PA Anton. Susceptibility of Lewis and Fischer rats to stress-induced worsening of TNB-colitis: protective role of brain CRF. **Am. J. Physiol.** 276:G1027-G1036, 1999.
28. Cole SW, ME Kemeny, OB Weitzman, M Schoen, PA Anton. Socially inhibited individuals show heightened DTH response during intense social engagement. **Brain Behav. Immun.** 13:187-200, 1999.
29. Rawsthorne P, F Shanahan, NC Cronin, PA Anton, R Löfberg, L Bohman, CN Bernstein. An international survey of the use and attitudes regarding alternative medicine by patients with inflammatory bowel disease. **Am. J. Gastroenterol.** 94:1298-1303, 1999.

30. Goode T, J O'Connell, P Anton, H Wong, J Reeve, GC O'Sullivan, JK Collins, F Shanahan. Neurokinin-1 receptor expression in inflammatory bowel disease: molecular quantitation and localization. **Gut** 47:387-396, 2000.

31. Mitsuyasu RT, PA Anton, SG Deeks, DT Scadden, E Connick, MT Downs, A Bakker, MR Roberts, CH June, S Jalali, AA Lin, R Pennathur-Das, KM Hege. Prolonged survival and tissue trafficking following adoptive transfer of CD4ζ gene-modified autologous $CD4^+$ and $CD8^+$ T cells in human immunodeficiency virus-infected subjects. **Blood** 96:785-793, 2000

32. Anton PA, J Elliott, MA Poles, IM McGowan, J Matud, LE Hultin, K Grovit-Ferbas, CR Mackay, ISY Chen, JV Giorgi. Enhanced levels of functional HIV-1 co-receptors on human mucosal T cells demonstrated using intestinal biopsy tissue. **AIDS** 14:1761-1765, 2000.

33. Olsson J, M Poles, A-L Spetz, J Elliott, L Hultin, J Giorgi, J Andersson, PA Anton. Human immunodeficiency virus type 1 infection is associated with significant mucosal inflammation characterized by increased expression of CCR5, CXCR4, and β-chemokines. **J. Infect. Dis.** 182:1625-1635, 2000.

34. Chang L, J Munakata, EA Mayer, MJ Schmulson, TD Johnson, CN Bernstein, L Saba, B Naliboff, PA Anton, K Matin. Perceptual responses in patients with inflammatory and functional bowel disease. **Gut** 47:497-505, 2000.

35. Poles MA, J Elliott, J Vingerhoets, L Michiels, A Scholliers, S Bloor, B Larder, K Hertogs, Anton PA. Despite high concordance, distinct mutational and phenotypic drug resistance profiles in human immunodeficiency virus type 1 RNA are observed in gastrointestinal mucosal biopsy specimens and peripheral blood mononuclear cells compared with plasma. **J. Infect. Dis.** 183:143-148, 2001.

36. Poles MA, M Fuerst, I McGowan, J Elliott, A Rezaei, D Mark, P Taing, PA Anton. HIV-related diarrhea is multifactorial and fat malabsorption is commonly present, independent of HAART. **Am. J. Gastroenterol.** 96:1831-1837, 2001.

37. Anton PA, MA Poles, J Elliott, SH Mao, I McGowan, H-J Lenz, ISY Chen. Sensitive and reproducible quantitation of mucosal HIV-1 RNA and DNA viral burden in patients with detectable and undetectable plasma viral HIV-1 RNA using endoscopic biopsies. **J. Virol. Methods**. 95:65-79, 2001.

B. RESEARCH PAPERS – Peer Reviewed - In Press

38. Poles MA, J Elliott, P Taing, PA Anton, ISY Chen. A preponderance of CCR5+, CXCR4+ mononuclear cells enhances gastrointestinal mucosal susceptibility to Human Immunodeficiency Virus Type 1 Infection. **J. Virol**. In Press.

C. RESEARCH PAPERS - Peer Reviewed- Submitted

39. Goldring AB, ME Kemeny, SE Taylor, PA Anton. An integrated model of treatment decision-making in chronic illness: impact of health beliefs, quality of life and the doctor-patient relationship on the treatment intentions of inflammatory bowel disease patients. **Health Psychology**, submitted, March 2000.

40. Keire D, PA Anton, KF Faull, E Ruth, JH Walsh, P Chew, D Quisimoro, M Territo, JR Reeve, Jr. Diethylphthalate: a chemotactic factor purified from supernatants of H. pylori. **J. Biol. Chem.**, submitted, December 2000.

D. RESEARCH PAPERS - Non Peer Reviewed

41. Anton PA, K Arnold, GK Truong, and WT Wong. Bacterial enteric pathogens in Vietnamese refugees in Hong Kong. **S.E. Asian J. Trop. Med. Pub. Health**, 12:151-156, 1981.

42. Thierman, D, JR Haaga, PA Anton, and JP LiPuma. Computed tomographic appearance of renal replacement lipomatosis. **J. Comput. Assist. Tomography** 7:341-343, 1983.

43. Anton PA, SR Targan, F Shanahan. F-Met-Leu-Phe induced chemiluminescence and binding in neutrophils from patients with inflammatory bowel disease. **Inflammatory Bowel Disease: Current Status and Future Approach**. Elsevier Science Publishers, New York. RP MacDermott, editor, pp 285-290, 1988.

44. Anton PA, JR Reeve, Jr., D Quismorio, K Smela, MC Territo, JH Walsh. Helicobacter pylori supernatant contains a novel chemotactic factor for monocytes and neutrophils different from **FMLP Helicobacter pylori: Basic Mechanisms**; New York, Elsevier Press, pp 198-206, 1994.

45. Anton PA. Be true to your stool: management of diarrhea that won't quit in HIV-positive patients. **POZ Magazine,** pp 84-85, November, 1997.

E. CHAPTERS

46. Anton PA, F Shanahan, JR Reeve, Jr. Biotinylated neuropeptide analogs: Design and use as probes for target cells in heterogeneous populations. **Methods in Neurosciences**, Conn PM, ed.; Orlando, Academic Press, vol. 13, pp: 76-90,1993.

47. Shanahan F, PA Anton. Role of peptides in the regulation of the mucosal immune and inflammatory response. **Gut Peptides: Biochemistry and Physiology**, Walsh JH, ed.; New York, Raven Press; pp: 851-867, 1994.

48. Anton PA. Stress and Mind-Body Impact on the Course of Inflammatory Bowel Disease. **Seminars in Gastrointestinal Dis.**, 10:14-19, 1999.

49. Cranston R, PA Anton, I McGowan. Gastrointestinal mucosal biopsy in HIV disease and AIDS. **Gastrointestinal Endoscopy Clinics of North America**, 10:637-667, 2000.

F. LETTERS TO THE EDITOR

50. Shanahan F, S Targan, PA Anton, R Duerr. Colonoscopy during an attack of severe ulcerative colitis. **Am. J. Gastroenterol.**, 86:1278, 1991.

51. Ilnyckyj A, F Shanahan, PA Anton, M Cheang, CN Bernstein. Therapeutic placebo in ulcerative colitis: Fact or fiction? **Gastroenterology**, 113:2021-2022, 1997.

52. Vidrich A, PA Anton, F Shanahan. Immuno-epithelial Interactions: Cytokine Modulation of Normal Rabbit Colonocyte Function. **In Vitro Cell Dev. Biol.**, 34:743-6, 1998.

G. PAPERS IN PREPARATION (research completed/near completion)

Manuscripts in final preparation or revision post submission:

53. Anton PA, M. Kemeny, M Schoen, K Horgan, S Fullerton, G Miller, F Moatamed. Modulatory effect of hypnosis in delayed-type hypersensitivity.
54. Weitzman, OB, SW Cole, ME Kemeny, PA Anton. Relationship between inhibited temperment and the immune system.
55. Anton PA, M Poles, J Elliott, S Brown. Comparative levels of HIV RNA and HIV DNA in compartments (gut mucosa and PBMC) over 12 months in subjects with undetectable viral load.

ABSTRACTS:

1. Anton PA, JA Kemp, T Butler, and MR Jacobs. Comprehensive efficacies of ceftriaxone, moxalactam and ampicillin in experimental *Salmonella typhimurium* infection. **International Conference on Antimicrobial Agents and Chemotherapy (ICAAC),** Chicago, 1981.
2. Anton PA, F Shanahan, M Durham, A Schwabe, and SR Targan. Enhanced sensitivity of neutrophils to f-Met-Leu-Phe in familial Mediterranean fever. **American Society for Clinical Investigation** 1987. (*Clinical Res.* 35: 639A, 1987).
3. Anton PA, F Shanahan, and SR Targan. Enhanced chemiluminescence in neutrophils from patients with IBD. **National Foundation for Ileitis and Colitis,** Int'l Conf., Fort Lauderdale, Florida, 1987.
4. Anton PA, SR Targan, F Shanahan. Neutrophil differences in FMLP-induced chemiluminescence and FMLP receptor number in patients with inflammatory bowel disease. **American Gastroenterological Association,** New Orleans, 1988. (*Gastroenterology* 94:A9, 1988).
5. Anton PA, JR Reeve Jr., W Schepp, F Shanahan. Biotinylation of a bombesin/gastrin releasing peptide analogue for use as a receptor probe. **Western Society for Clinical Investigation,** Carmel, 1990 (*Clin Res* 38:A148,1990).
6. Anton PA, JR Reeve Jr., A Vidrich, E Mayer, F Shanahan. Biotinylated analogues of substance P to identify receptors in mixed cell populations. **American Gastroenterological Association,** San Antonio, 1990 (*Gastroenterology* 98:A482, 1990).
7. Mayer E, PA Anton, F Shanahan, A Kodner. VIP-activated membrane channels mediate calcium influx in human Molt 4b lymphoblasts. **Second International Conference on Gastroenteric Biology,** Chicago, 1989.
8. Sun XP, EA Mayer, F Shanahan, PA Anton, A Kodner. Regulation of intracellular calcium in Molt 4b lymphoblasts. **FASEB Meeting,** Washington, D.C., 1990 (*FASEB* 4:A5435, p1202, 1990).
9. Mayer E, XP Sun, PA Anton, F Shanahan, A Kodner. VIP regulates intracellular calcium in Molt 4b lymphoblasts. **American Gastroenterological Association,** San Antonio, 1990. (*Gastroenterology* 98:A509, 1990).
10. Martin FC, PA Anton, JA Gornbein, F Shanahan, JE Merrill. Substance P receptors on microglia. **ASBMB/AAI,** New Orleans, 1990.
11. Vidrich A, PA Anton, F Shanahan. Growth enhancement of normal colon epithelial cells by TNF and IL-1. **Gastroenteric Biology Conference,** Chicago, 1990.

12. Vidrich A, PA Anton, F Shanahan. Cytokines modulate the growth of normal colonic epithelia. **American Gastroenterological Association,** New Orleans, 1991. (*Gastroenterology* 100:A623, 1991).

13. Anton PA, F Shanahan, D Mall, A Vidrich. Characterization of receptors for gastrin-releasing peptide on normal canine colonic epithelia. **American Gastroenterological Association,** San Francisco, 1992. (*Gastroenterology* 102:A719, 1992).

14. Bernstein CN, F Shanahan, PA Anton, WM Weinstein. Patchy involvement, including rectal sparing, occurs in ulcerative colitis: a prospective study. **American Gastroenterological Association,** Boston, 1993 (*Gastroenterology* 104:A668, 1993).

15. Bernstein CN, LL Seeger, JW Sayre, PA Anton, L Artinian, F Shanahan. Osteopenia in inflammatory bowel disease (IBD) is related to prednisone use and not disease diagnosis: a prospective study. **American Gastroenterological Association,** Boston, 1993 (*Gastroenterology* 104:A668, 1993).

16. Anton PA. Inflammatory Bowel Disease (IBD): the role of psychoneuroimmunology in chronic illness. **North American Primary Research Group,** San Diego, CA, 1993. (*NAPCRG,* A149, p131, 1993).

17. Mitrovic B, FC Martin, AC Charles, LJ Ignarro, PA Anton, F Shanahan, JE Merrill. Neurotransmitters and cytokines in CNS pathology. **Fifth International Symposium on Neural Regulation,** Asilomar, CA, December 1993.

18. Anton PA, JR Reeve, D Quismorio, K Smela, MC Territo, JH Walsh. *Helicobacter pylori* supernatant contains a novel chemotactic factor for monocytes different from FMLP. **American Gastroenterological Association,** New Orleans, 1994 (*Gastroenterology* 106:A 40, 1994)

19. Anton PA, KH Horgan, F Espin, F Shanahan. Mechanism of substance P receptor upregulation in human mucosal inflammation. **American Gastroenterological Association,** San Diego, CA, 1995. (*Gastroenterology* 108:A772, 1995).

20. Bernstein CN, LL Seeger, PA Anton, L Artinian, WG Goodman, SP Geffrey, T Belin, F Shanahan. Oral calcium and vitamin D do not impact on decreased bone density in inflammatory bowel disease (IBD): a prospective randomized placebo-controlled study. **American Gastroenterological Association,** San Diego, CA, 1995. (*Gastroenterology* 108:A782, 1995).

21. McGowan I, M Miller, E Wager, PA Anton. Diagnosis of cytomegalovirus (CMV) infections in patients with HIV associated gastrointestinal disease. United Kingdom Medical Research Council Annual Meeting, Oxford, England, September, 1995.

22. McGowan I, F Shanahan, K Horgan, PA Anton. Substance P receptor (SPR) expression in HIV-infected intestinal mucosa. **United Kingdom Medical Research Council Annual Meeting,** Oxford, England, 9/95.

23. Anton PA, J O'Connell, D O'Connell, F O'Brian, JK Collins, GC O'Sullivan, F Shanahan. Distribution of receptors for the chemotactic peptide, FMLP, in colonic mucosa. **American Gastroenterological Association,** San Francisco, CA, 1996. (*Gastroenterology* 110:A856, 1996).

24. Ilnyckyj A, F Shanahan, PA Anton, CN Bernstein. The placebo response in ulcerative colitis. **American Gastroenterological Association,** San Francisco, CA, 1996. (*Gastroenterology* 110:A929, 1996).

25. McGowan I, K Horgan, PA Anton. Cytokine profiles in inflammatory bowel disease. **American Gastroenterological Association,** San Francisco, CA, 1996. (*Gastroenterology* 110:A962, 1996).

26. McGowan I, M Miller, D Lewin, E Wager, K Horgan, PA Anton. Diagnosis of cytomegalovirus (CMV) infection in patients with HIV-associated gastrointestinal disease.

American Gastroenterological Association, San Francisco, CA, 1996. (*Gastroenterology* 110:A963, 1996).

27. McGowan I, Y Li, A Kaplan, K Horgan, PA Anton. Is diagnostic endoscopy associated with increases in viral load in HIV-1 infected patients? **American Gastroenterological Association**, San Francisco, CA, 1996. (*Gastroenterology* 110:A963, 1996).
28. Mulugeta M, PA Anton, Y Tache. Chronic stress potentiates TNB-induced colitis differentially in female Lewis and Fischer rats. **American Gastroenterological Association**, San Francisco, CA, 1996. (*Gastroenterology* 110:A969, 1996).
29. McGowan I, F Shanahan, K Horgan, PA Anton. Substance P receptor expression in intestinal mucosa. **American Gastroenterological Association**, San Francisco, CA, 1996. (*Gastroenterology* 110:A1099, 1996).
30. McGowan I, Y Li, PA Anton, A Kaplan. Diagnostic endoscopy in HIV-infected patients: no increase in viral load. **Third Conference on Retroviruses and Opportunistic Infections**, Washington, DC, 1996.
31. McGowan I, M Miller, D Lewin, E Wager, K Horgan, PA Anton. (Updated) Diagnosis of cytomegalovirus (CMV) infection in patients with HIV-associated gastrointestinal disease. **XI International Conference on AIDS**, Vancouver, Canada, 1996.
32. McGowan I, Y Li, A Kaplan, K Horgan, PA Anton. (Updated) Is diagnostic endoscopy associated with increases in viral load in HIV-1 infected patients? **XI International Conference on AIDS**, Vancouver, Canada, 1996.
33. Chalmers A, I McGowan, F Shanahan, PA Anton. Substance P receptor expression in HIV-infected intestinal mucosa is decreased. **XI International Conference on AIDS**, Vancouver, Canada, 1996.
34. Goode T, J O'Connell, PA Anton, I McGowan, JK Collins, GC O'Sullivan, F Shanahan. Development of a competitive rt-PCR system for quantification of substance P receptor mRNA expression in inflammatory and other bowel diseases. **Irish Society of Gastroenterology**, Dublin, 1995. (*Irish Journal of Medical Science* 165:21, 1995)
35. Mulugeta M, PA Anton, Y Tache. Stress induced worsening of colonic inflammation: protective role of brain CRF in experimental colitis in Fischer and Lewis Rats. **American Gastroenterological Association**, Washington, DC, 1997. (*Gastroenterology* 112:A1043, 1997).
36. Anton PA, M Schoen, E Mayer, S Fullerton, C Landes, K Horgan, ME Kemeny. Hypnosis not directed at specific symptoms fails to improve irritable bowel symptoms. **American Gastroenterological Association**, Washington, DC, 1997. (*Gastroenterology* 112:A692, 1997).
37. Xiong YP, A Udalve, M Chang, L Leichamn, RW Beart, PA Anton, HJ Lenz. Thymidylate synthase (TS), Cox-1 and COS-2 gene expression levels in active and inactive mucosae in patients with inflammatory bowel disease. **American Association for Cancer Research**, New Orleans, LA, 1998 (*Proc Am Assn Cancer Res* 39:488; A3319)
38. Elliott J, L Hultin, MA Poles, J Giorgi, PA Anton. Chemokine receptor expression is increased on mucosal versus blood CD4+ T cells". **American Gastroenterological Association**, New Orleans, LA, 1998. (*Gastroenterology* 114:AG3983).
39. Poles MA, E Martin-Porter, JS Lee, J Naitoh, PA Anton, T Ganz. What can urine teach us about intestinal defense? **American Gastroenterological Association**, New Orleans, LA, 1998. (*Gastroenterology* 114:AG4340).
40. Rawsthorne P, F Shanahan, CC Cronin, PA Anton, R Lofberg, CN Bernstein. An international survey of the use and attitudes regarding alternative medicine by patients with inflammatory bowel disease (IBD). **American Gastroenterological Association**, New Orleans, LA, 1998. (*Gastroenterology* 114:AG4368).

41. Million M, A Belai, Y Akiba, PA Anton, Y Tache. Chronic stress-induced worsening of chronic colonic inflammation in Lewis rats involves colonic mast cells degranulation. **American Gastroenterological Association**, New Orleans, LA, 1998. (*Gastroenterology* 114:AG4697).

42. Fullerton S, PA Anton, L Chang, B Naliboff, CN Bernstein, EA Mayer. Prevalence of extraintestinal symptoms in patients with irritable bowel syndrome and inflammatory bowel disease. **American Gastroenterological Association**, New Orleans, LA, 1998. (*Gastroenterology* 114:AG0059).

43. Weitzman OB, SW Cole, ME Kemeny, PA Anton. Relationship between inhibited temperament and the immune system. **American Psychological Association**, San Francisco, CA, 1998.

44. PA Anton, J Elliott, M Poles, SH Mao, HJ Lenz, I McGowan, K Hege, D Ando, ISY Chen. Quantitative assessment of tissue viral burden using a single intestinal biopsy. **2nd International Workshop on HIV Drug Resistance & Treatment Strategies**, Lake Maggiore, Italy, June 1998.

45. PA Anton, J Elliott, M Poles, L Hultin, C Mackay, J Giorgi. Increased expression of chemokine co-receptors on mucosal versus circulating CD4+ T cells in seronegative controls. **12th World AIDS Conference**, Geneva, Switzerland; June 1998.

46. K Hege, S Deeks, R Mitsuyasu, PA Anton, D Scadden, L Connick, MR Roberts. Improved survival and tissue trafficking of CD4-zeta, gene-modified T cells in HIV-infected subjects by co-infusion of HIV-specific CD4 and CD8 T cells. **12th World AIDS Conference**, Geneva, Switzerland; June 1998.

47. Deeks S, R Mitsuyasu, D Scadden, L Connick, PA Anton, D Broad, K Hege. Adoptive immunotherapy of HIV infection with autologous CD4-zeta, gene-modified CD4 and CD8 T cells. **ICAAC**, San Diego, CA; October 1998.

48. M Poles, J Elliott, DP Shi, J Giorgi, L Hultin, ISY Chen, PA Anton. Mucosal mononuclear cells (MMC) are more infectable with HIV in vitro than peripheral blood mononuclear cells (PBMC). **6th Conference on Retroviruses and Opportunistic Infections**, Chicago, IL; January 1999.

49. M Poles, J Elliott, S Brown, DP Shi, S Chiong, K Hege, I McGowan, HJ Lenz, ISY Chen, PA Anton. HIV-1 is detectable in mucosal biopsies in patients with undetectable plasma viral loads. **6th Conference on Retroviruses and Opportunistic Infections**, Chicago, IL; January 1999.

50. Hege K, B Wagner, R Mitsuyasu, PA Anton, D Scadden, S Kwok, R Lazar, R Pennathur-Das, S Deeks. HIV-specific T cell gene therapy in subjects with undetectable viremia on HAART. **6th Conference on Retroviruses and Opportunistic Infections**, Chicago, IL; January 1999.

51. Anton PA, L Michiels, J Vingerhoets, A Scholliers, M Poles, J Elliott, D Mark, DP Shi, P Stoffels, B Larder, K Hertogs. Comparative patterns of HIV-1 genotypic and phenotypic resistance in gut and plasma. **3rd International Workshop on HIV Drug Resistance and Treatment Strategies**, San Diego, CA; June 1999.

52. Hege K, B Wagner, R Mitsuyasu, P Anton, D Scadden, S Kwok, C Macken, S Deeks. HIV-specific T cell gene therapy suppresses viral load rebound in subjects on highly active antiretroviral therapy (HAART): A randomized controlled trial. **7th Conference on Retroviruses and Opportunistic Infections**, San Francisco, CA; January 2000.

53. Olsson J, A-L Spetz, PA Anton, J Andersson. "CD40L is downregulated and CTLA-4 is upregulated in gut mucosa in HIV-infected patients. **7th Conference on Retroviruses and Opportunistic Infections**, San Francisco, CA; January 2000.

54. Olsson J, A-L Spetz, M Poles, J Elliott, J Andersson, PA Anton. HIV infection is associated with significant mucosal inflammation. **7th Conference on Retroviruses and Opportunistic Infections**, San Francisco, CA; January 2000.

55. Poles M, J Elliott, D Mark, P Tiang, A Raezai, PA Anton. 5-aminosalicylic acid suppresses HIV replication *in vitro*. **3rd Annual Conference on AIDS Research in California, UARP**; San Francisco, CA, February 2000.

56. Poles M, J Elliott, D Mark, P Taing, J Ingerhoets, L Michiels, B Larder, K Hertogs, A Scholliers, PA Anton. HIV resistance profiles in the gastrointestinal mucosa can be determined from rectosigmoid biopsies. **American Gastroenterology Association**, San Diego, CA; May 2000.

57. Poles M, J Elliott, J Ollsson, J Andersson, PA Anton. Inflammatory bowel disease is characterized by elevated tissue concentrations of beta-chemokines and altered chemokine receptor expression. **American Gastroenterology Association**, San Diego, CA; May 2000.

58. Poles M, A Rezaei, M Fuerst, PA Anton. High prevalence of steatorrhea in HIV patients with diarrhea regardless of HAART use. **American Gastroenterology Association**, San Diego, CA; May 2000.

59. Vingerhoets J, MA Poles, L Michiels, J Elliott, S Bloor V De Vroey , P Dehertogh, B Larder, K Hertogs, PA Anton. RT and protease mutations and phenotypic HIV-1 drug resistance in gastrointestinal mucosa and plasma. **4th International Workshop on HIV Drug Resistance and Treatment Strategies**, Sitges, Spain; June 2000.

60. Boscardin WJ, J Elliott, M Poles, P Taing, S Brown, M Fuerst, M Kemeny, J Matud, P Anton. Reliability and Correlations of Repeated Viral Load Measures in Plasma and Gut Mucosa (GALT) to determine baseline characteristics in clinical trials. **8th Conference on Retroviruses and Opportunistic Infections,** Chicago, IL; February 2001. [abstract O38e].

61. Elliott J, D Mark, M Fuerst, P Taing, A Rezaei, M Poles, S Brown, P Anton. HIV-1 DNA is persistently detectable in gastrointestinal mucosa in subjects with undetectable plasma viral load over 3 years. **8th Conference on Retroviruses and Opportunistic Infections**, Chicago, IL; February 2001. [abstract D81e].

62. Poles MA, J Elliott, P Taing, PA Anton, ISY Chen. Phenotypic differences between the mucosal environment and blood likely account for greater permissiveness for HIV in the gut. **American Gastroenterology Association,** Atlanta, GA, May 20 – 23, 2001 [abstract 2621].

63. Poles MA, L O' Mahony, J Elliott, P Taing, PA Anton, ISY Chen. Mucosal epithelial cells modulate pro-inflammatory cytokine production in response to pathogenic bacteria and influences mucosal HIV replication. **American Gastroenterology Association**, Atlanta, GA, May 20 – 23, 2001 [abstract 999].

64. Anton PA M Fuerst, J Elliott, J Matud, J Boscardin, M Kemeny, M Poles. Pilot study of 5-ASA mucosal anti-inflammatory medication as adjunctive therapy to HAART in decreasing mucosal, and plasma viral load. **1st IAS Conference on HIV Pathogenesis and Treatment**, Buenos Aires, Argentina, July 2001. [abstract 1085].

65. Anton PA J Elliott, M Quigley, J Olsson, P Taing, M Kemeny, M Poles. Use of Asacol®, a mucosal anti-inflammatory medication, is safe as adjunctive HIV therapy and is associated with mild decreases in mucosal RANTES. **1st IAS Conference on HIV Pathogenesis and Treatment**, Buenos Aires, Argentina, July 2001. [abstract 1081].

66. Vingerhoets J, MA Poles, J Elliott, R Harrigan, B Lader, P McKenna, K Hertogs, PA Anton. HIV RNA from gastrointestinal mucosa shows similar RT and protease mutations and phenotypic HIV-1 drug resistance as plasma-derived HIV. **5th International Workshop on HIV Drug Resistance and Treatment Strategies**, Scottsdale, AZ, June 2001.

67. Vingerhoets J, MA Poles, J Elliott, R Harrigan, B Larder, P McKennal, K Hertogs, PA Anton. HIV RNA from gastrointestinal mucosa shows similar RT and protease mutations

and phenotypic HIV-1 drug resistance as plasma-derived HIV. **41st ICAAC Meeting,** Chicago, Illinois, September 2001.

PATENTS

1. Anton, Shanahan, Reeve
   Biotinylated neuropeptides
   US Patent application #07/860,405 (3/30/92)
2. Anton, Reeve, Walsh, Faull
   Helicobacter pylori bacterial derived factor
   US Patent application #08/395,495 (2/23/95)
3. Anton, Poles, Elliott, Giorgi
   Anti-inflammatory therapy for inflammatory mediated infection
   US Patent application #31,678 (5/14/99)
4. Anton, McGowan, Elliott, Chen
   Determining nucleic acid sequences in a biological sample
   US Patent application #US99/14366 (6/24/99)

INVITED LECTURES (selected)

National Foundation for Ileitis and Colitis
Los Angeles, CA; August 1991.
"The Status of Stress in the Clinical Course of IBD"

National Foundation for Ileitis and Colitis
Brentwood, CA; May, 1990.
"Research Updates in IBD: Information for Young Adults"

Holy Cross Hospital
Mission Hills, CA; October, 1992.
"Medical Management of Inflammatory Bowel Disease"

Psoriasis Research Institute
Palo Alto, CA; February, 1993.
"Role of substance P in gut inflammation: parallels for skin"

UCLA Inflammatory Bowel Disease CME Course
Los Angeles, CA; February, 1993.
"New Clinical Research Frontiers in IBD"

Kern Medical Center
Bakersfield, CA; October, 1993.
"Current Management of Inflammatory Bowel Disease"

UCLA Family Practice Grand Rounds
Los Angeles, CA; November, 1993.
"Primary Care Management of Inflammatory Bowel Disease"

North American Primary Research Group
San Diego, CA; November, 1993.
"Inflammatory Bowel Disease (IBD): The role of psychoneuroimmunology in chronic illness"

UCLA Medical Grand Rounds
Los Angeles, CA; August, 1994.
"New Frontiers in the Management of Inflammatory Bowel Disease"

World Congress in Gastroenterology: Young Clinicians Forum
Los Angeles, CA; October 1994
"Management Approaches and Research Directions in IBD in the USA"

Royal College of Physicians and Surgeons, Ireland
Cork, Ireland; March 1995.
"Alternative Medicine in the USA: A perspective"

International AIDS Symposium
Los Angeles, CA; March, 1995.
"Diagnosis and Management of HIV-Related Diarrhea"

Inflammatory Bowel Disease FORUM, American Gastroenterology Association Conference
San Diego, CA; May, 1995.
"Antibiotic Treatment for Inflammatory Bowel Disease"

Grand Rounds, Hoag Hospital
Newport Beach, CA; August, 1995.
"Difficult Management Decisions in IBD"

New Orleans Gut Club/CCFA Chapter
Covington, LA; August, 1995.
"What's beyond steroids: new options in managing IBD"

AIDS-Manasota "Until there is a Cure" Conference
Sarasota, Florida; January, 1996.
"The multifactorial nature of AIDS-related diarrhea"

Conant Foundation: Community Forum
San Francisco, CA; April, 1996.
"Management of HIV-related diarrhea for the patient: A discussion of causes and treatments"

UCLA Department of Medicine: Housestaff Conference
Los Angeles, CA; April, 1996.
"The ABC's of IBD"

UCLA Medical School: Course "Introduction to Complimentary Medicine"
Los Angeles, CA; April, 1996.
"Psychoneuroimmunology and the placebo effect in medicine"

Norman Cousins Program in Psychoneuroimmunology: Public Information Event
Los Angeles, CA; April, 1996.
"Neuroimmunomodulation: the biology of how it works"

UCLA Medical School: Course "Pathophysiology of GI Disease"
Los Angeles, CA; April, 1996.
"Gastrointestinal Flora"

National University of Ireland: 1st Annual Mind-Body Symposium
Cork, Ireland; March, 1997.
"The role of neuropeptides and mind/body in modulation of intestinal inflammation"

American College of Surgeons Clinical Congress 1997.
Chicago, Ill; October 1997.
"Medical management of inflammatory bowel disease: rationale and updates"

National Forum for AIDS Management: Conant Foundation
Scottsdale, AZ; October, 1997.
"Management of HIV-related diarrhea"

Mind-Body Seminar: Public Information Event (organizer)
UCLA, Los Angeles, CA; November, 1997.
"The effects of hypnosis and education on health"

AIDS Clinical Trial Group (ACTG) Immunology RAC
San Diego, CA; April, 1998.
"Mucosal HIV pathogenesis: viral load and flow cytometry"

Research Forum for GI Endoscopic Nurses
Los Angeles, CA; June, 1998.
"Frontiers in the role of endoscopy in HIV research"

AIDS ReSearch Alliance: Patient Information Series
Los Angeles, CA; September, 1998.
"The role of endoscopic biopsies in evaluating total body viral load of HIV"

Rush Medical School; Department of Immunology
Chicago, Ill; October, 1998.
The importance of the gut (GALT) in HIV Disease: Access, Acquisition and Inflammation"

National University of Ireland: 2nd Annual Mind-Body Symposium
Galway, Ireland; October, 1998.
"Stress modulates the inflammatory response in IBD"

Being Alive Foundation
Torrance, CA; November, 1998.
"What you can do in managing HIV-related diarrhea"
"New frontiers in HIV Research: The role of tissue and endoscopic biopsies"

UCLA Pathology Grand Rounds
Los Angeles, CA, May, 1999.
"Advances in understanding the impact of HIV in the gut"

AIDS Healthcare Foundation (AHF)
Los Angeles, CA; June, 1999.
"Clinical implications of HIV's activity in the gut: detection and treatment"

UCLA Immunology Training Program
Los Angeles, CA; June, 1999.
"Substance P and immune modulation: new tools for detection"

San Diego HIV-Treating Physicians Forum
San Diego, CA; July, 1999.
"The multifactoral approach to diagnosing and treating HIV-related diarrhea"

ACTG: Mucosal Immunology Focus Group (Immunology RAC)
Washington, D.C.; July, 1999.
"Quantitative assays for detecting HIV RNA and DNA in gut tissue"

UCLA Division of Digestive Diseases: Staff retreat
Los Angeles, CA; November, 1999.
"HIV and the gut: a new frontier for research and patient care"

California AIDS Research Centers 3rd Annual Meeting
San Diego, CA; May, 2000
"GI –based immuno strategies for an HIV Vaccine"

AIDS Project Los Angeles (APLA)
Los Angeles, CA; September, 2000
"Diarrhea in HIV-patients: Why is it still a problem?"

Chromavision, Inc.
San Juan Capistrano, CA; September, 2000
"Role of quantitative imaghe analysis in determining HIV tissue viral burden"

Einstein Annual Honors Lecture
Bakersfield, CA; March 2001
"HIV and the gut: a new frontier"

UCLA Neuropsychiatric Institute & Hospital
Los Angeles, CA; March 2001
"Mucosal immunology: oral tolerance and vaccines"

UCLA Alumni Association
Manhattan Beach, CA; April 2001
"UCLA's Quest for an AIDS Vaccine"

UCLA School of Medicine
Los Angeles, CA; April 2001
"The Gut: A primary site for HIV infection, prevention and treatment"

Chicanos/Latinos for Community Medicine
Los Angeles, CA; April 2001
"Current trends in HIV vaccine research"

American Federation for Medical Research
Los Angeles, CA; May 2001
"Career Opportunities in Clinical Investigation"

Axcan Scandiopharm, Inc.
San Francisco, CA; June, 2001
"Title????HIV-related diarrhea???"

(5)

PATENT

Docket No. 1377-0137P

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS: John Kevin Collins *et al.*

APPLN. NO.: 09/367,105 GROUP: 1651

FILED: November 10, 1999 EXAMINER: L Marx

FOR: PROBIOTIC STRAINS FROM LACTOBACILLUS SALIVARIUS AND ANTIMICROBIAL AGENTS OBTAINED THEREFROM

DECLARATION UNDER 37 C.F.R. § 1.132

Assistant Commissioner of Patents

Washington, DC 20231

Sir:

I, John Kevin Collins, am presently employed as Vice President for Research and as Associate Professor in the Departments of Medicine and Microbiology, at University College Cork - National University of Ireland, Cork, College Road, Cork, Ireland. My *Curriculum Vitae* is attached hereto. I do solemnly and sincerely declare as follows:

1. I am authorized to make this Declaration on behalf of the Applicants.

2. I am an inventor in respect of the above Application and I attended at an interview with the Examiner on January 17, 2003.

During the interview, which was also attended by Mr. Eugene Perez and Dr. MaryAnne Armstrong of the firm Birch Stewart Kolasch & Birch LLP, the invention was discussed and it was agreed that amended claims would be filed and these were filed by way of a Supplemental Amendment on January 22, 2003.

3. As requested by the Examiner, I have given further consideration to certain definitions queried by her, namely the terms "mutant", "variant" and "closely related bacteria" as used in the context of the present invention.

4. As regards a definition of a variant/mutant, it was agreed at the interview that variants were inclusive of mutants. In addition I stated that variants could include extra-chromosomal genetic elements, e.g. plasmids, transposons, bacteriophage, which would genotypically and phenotypically add new properties to a strain without mutation or changing the base sequence of the bacterial genome. As I recall it was agreed after a detailed discussion at the interview that the term "variant" was the most comprehensive and suitable definition currently available.

5. As regards the definition of "closely related bacteria", I would refer to previous submissions filed during the course of prosecution of this Application. I would also stress that bacteriocins have classically been described as secreted proteinaceous factors that inhibit similar strains to that of the strains produced or other closely related strains. In this context,

it would imply that ABP 118 produced by UCC 118 as described in the specification of the present Application would inhibit other *Lactobacillus salivarius* strains and other lactobacilli strains. This implies that phylogenetically similar strains are closely related. Specifically, lactic acid bacteria (lactococci, bifidobacteria and pediococci) can be considered as being closely related to each other. As outlined in the Application ABP118 does not inhibit any of the closely related strains (i.e. other lactic acid bacteria) with one exception (i.e. *Lactobacillus fermentum* KLD). ABP118 clearly inhibits strains far removed from lactobacillus on the phylogenetic tree. Thus closely related bacteria specifically relates to other lactic acid bacteria.

6. I also wish to comment on the matter of the selection of adherent strains as discussed with the Examiner Dr. Marx during the interview. As I advised the Examiner we are in possession of a suite of lactobacillus strains selected from washed gastrointestinal tissue. *In vitro* adhesion assays illustrate that all of these strains adhere to human gastrointestinal epithelial cell lines (Caco-2 and HT-29). This is in contrast to strains isolated from other environments, e.g. dairy products. Direct comparisons with commercially available strains, the majority of which are faecal in origin, show that the strains isolated from the human gut have superior adherence properties. While we have isolated a suite of strains in this way, for resource reasons

we have focused our research on two strains, namely UCC1 and UCC118.

7. I also advised the Examiner that in subsequent research I have screened thousands of faecal lactobacillus isolates from a number of volunteers and have failed to find strains with similar anti-microbial profiles of UCC1 and UCC118. This is further proof that isolation of strains from washed and resected tissue provides access to strains with specific properties. These confer a selective survival advantage to the strain within the human gastrointestinal tract. Further ongoing research is confirming these results. I also advised the Examiner that bacterial strains that colonise the human gut are specifically adapted (humanized) to a unique microenvironment which may be the result of thousands of years of co-evolution. This was illustrated in human feeding studies where UCC118 is the only strain known to colonize a human volunteer for greater than one hundred days following cessation of feeding. This unique finding supports the case that strains isolated in this manner (from resected and washed human gastrointestinal tract) have unique abilities to adhere, survive and compete in the complex milieu of microbes, mucins and mucosal immune system that is the human gastrointestinal tract.

I hereby declare that all statements made herein of my own knowledge are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

February 18, 2003
Date

John Kevin Collins, Ph.D.

NAME: John Kevin Collins

POSITION: Vice-President for Research, University College Cork
Associate Professor in Departments of Medicine & Microbiology
University College Cork

QUALIFICATIONS

1970	BSc (Biochemistry/Microbiology), University College Cork
1974	PhD (Biochemistry/Microbiology), National University of Ireland

Brief Outline of Academic History

1995-present	Associate Professor, Depts. of Medicine & Microbiology, UCC
1992-1995	Associate Professor, Dept. of Microbiology, UCC
1983-1992	Senior Lecturer, Dept. of Microbiology, UCC
1977-1983	College Lecturer, Dept. of Microbiology, UCC
1982-1983	Visiting Research Professor, Bacteriology Department, University of California at Davis, USA
1976-1977	Post-Doctoral Research Fellow, Depts. of Pathology & Bacteriology, University of California at Davis, USA
1975-1976	NIH Post-Doctoral Research Fellow, Department of Microbiology, Health Science Center, State University of New York at Stony Brook, New York, USA
1974-1975	Damon Runyon Cancer Research Fund Post-Doctoral Fellow, Depts. of Pharmacology and Anatomy, Case Western Reserve University Medical School and Hospital, Cleveland, Ohio, USA
1970-1974	PhD Graduate Student, University College Cork.

RESEARCH INTERESTS

- Gastroenterology
- Gut Flora – including hitherto unculturables.
- Interaction of the gut flora with the mucosal immune system in health and disease.
- Inflammatory Bowel Disease – both Crohn's Disease and Ulcerative Colitis.
- Gastrointestinal Cancer.
- Probiotics as new therapeutic sources, e.g. from bugs to drugs.
- Taking probiotics from bench to bedside.
- Elucidating mechanisms of action of scientifically proven probiotic action.
- Virology – new antiviral agents.

Number of peer reviewed publications: 110+

Number of completed graduate student theses: 20 PhD; 18 MSc

Research funding generated: €6.2 m
(Individually and with colleagues)

Selected Research Publications:

Flynn, S., van Sinderen, D., Thornton, G.M., Holo, H., Nes, I.F. & Collins, J.K.
Characterisation of the genetic locus responsible for the production of ABP-118, a novel bacteriocin produced by the probiotic bacterium *Lactobacillus salivarius* subsp. *salivarius* UCC118.
Microbiology, 2002. Apr; 148 (Pt. 4): 973-84.

Fanning, L., Loane, J., Kenny-Walsh, E., Sheehan, M., Whelton, M., Kirwan, W., Collins J.K. & Shanahan, F.
Tissue viral load variability in chronic hepatitis C.
Am. J. Gastroenterol. 2001 Dec; 96(12): 2284-9.

O'Sullivan, G., Ryan, P., Aarons, S., Walsh, T., Sheahan, D., Collins, J.K., &Shanahan, F. 2001.
Bone marrow micrometastasis in esophageal cancer : incidence and response to chemotherapy.
Recent Advances in Disease of the Esophagus 8: 385-388.

Aarons, S., Ryan, P., O'Sullivan, G., Sheahan, D., Collins, J.K. & Shanahan, F. 2001.
Stable expression of transgenes in esophageal cancer : implication for development of gene therapy. International Society for Diseases of the Esophagus 8: 403-407.

Bennett, M.W., O'Connell, J., Houston, A., Kelly, J., O'Sullivan, G.C., Collins, J.K. & Shanahan, F.
Fas ligand upregulation is an early event in colonic carcinogenesis.
J. Clin. Pathol. 2001. Aug; 54 (8): 598-604.

O'Mahony, L., Feeney, M., O'Halloran, S., Murphy, L., Kiely, B., Fitzgibbon, J., Lee, G., O'Sullivan, G., Shanahan, F. & Collins, J.K.
Probiotic impact on microbial flora, inflammation and tumour development in IL-10 knockout mice.
Aliment Pharmacol Ther. 2001. Aug; 15(8): 1219-25.

Barry, O.P., Mullan, B., Sheehan, ,D., Kazanietz, M.G., Shanahan, F., Collins, J.K. & O'Sullivan, G.C.
Constitutive ERK 1/2 activation in esophagogastric rib bone marrow micrometastatic cells is MEK-independent.
J. Biol. Chem. 2001 May 4; 276(18): 15537-46.

Dunne, C., O'Mahony, L., Murphy, L., Thornton, G., Morrissey, D., O'Halloran, S., Feeney, M., Flynn, S., Fitzgerald, G., Daly, C., Kiely, B., O'Sullivan, G.C., Shanahan, F. & Collins, J.K.
In vitro selection criteria for probiotic bacteria of human origin : correlation with *in vivo* findings.
Am. J. Clin. Nutr. 2001 Feb; 73: 386-392.